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CASE OF RECOVERY

FROM A

POISONOUS DOSE OF STRYCHNIA;

WITH OBSERVATIONS ON THE TESTS FOR ORGANIC ALKALIES.

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Mr B. has been afflicted, for a considerable period, with tic douloureux, occurring at irregular intervals, and in paroxysms of excessive violence. For the relief of the pain of these attacks he has been in the habit of making use of muriate of morphia, at first in small quantities, and afterwards in gradually increased doses, until three and a half grains were necessary to produce its effect. At this time, he went into the shop of a druggist in the town in which he resided, for the purpose of obtaining some muriate of morphia, and received a quantity of a powder slightly yellowish in colour, which was stated to be that substance. On the same day, having occasion to go a short distance into the country on business, he took, previous to going out, his usual dose, 3½ grains of the powder, which was simply placed upon the tongue and swallowed, and he remarked at the time that it was extremely bitter, and that the taste was more than usually persistent, but it did not occur to him that any thing was wrong. Shortly after, however, while walking along the street, he felt slightly indisposed, the most prominent symptom being a sense of numbness in the back of the legs, which he attributed to the effects of cold, to which he had been exposed in the early part of the morning. As these symptoms did not appear of any importance, he proceeded by a public conveyance to the village where his business lay, and returned by the next opportunity. During the whole of this time the symptoms remained precisely as they were the moment he first observed them; but as he was walking along, on his return, they suddenly increased, the numbness being accompanied by a sense of want of power, and a sort of dragging of the muscles of the legs, which soon became so great, that, as he describes it, he had to put his hands at the back of his thighs in order to push his legs along. This

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occurred at nearly two and a half hours after he had taken the dose of the supposed muriate of morphia, and, at this time, there could have been nothing remarkable or unusual in his appearance; for, on his way home, he met a friend to whom he communicated his sensations, but who laughed at his evident apprehension, and assured him that it was all imagination. As he was in the midst of describing the effect upon his muscles, and bending himself so as to show how it occurred, he suddenly overbalanced and fell heavily backwards. He was immediately raised, and, on attaining the upright position, he felt himself much in the same state in which he was before, excepting that he was excessively nervous and alarmed. The want of power in the legs did not at all increase in intensity, and no spasmodic affection was observed, although the patient was himself under the impression, that his fall was somehow connected with the previous symptoms.

The patient's fall and the nervous state into which he had got, now fairly alarmed his friend, who begged him to get home as fast as possible, and accompanied him on his way, as he experienced considerable difficulty in walking, and could not get on without support. On reaching home he felt somewhat better, and remained sitting for some time, and at length retired to bed, about five hours after the first appearance of the symptoms. Just previous to stepping into bed, in order to insure a good night's rest, of which the recent symptoms rendered him somewhat doubtful, he took a second dose of the powder equal in amount to the first. In less than ten minutes after, he was seized with a violent tetanic spasm, affecting the legs and muscles of respiration, and had only time to call out for assistance before the sensation amounted to that of absolute suffocation. Fortunately, assistance was close at hand, and he was immediately raised up in bed, with the effect of entirely relieving the sense of suffocation, and a medical man sent for. Spasms now followed each other in rapid succession, the intervals being about a quarter of an hour or twenty minutes, and the affection was confined principally to the legs, back, and respiratory muscles, the arms being comparatively unaffected. The numbness and dragging of the muscles, which had been continuous during the first five hours, disappeared entirely during the intervals of the spasms, and the patient was left without any uneasy sensations, excepting the exhaustion of the previous fit and the apprehension of its successor. During the whole of this time he was not only perfectly conscious, but his senses were preternaturally exalted, and he distinctly heard a variety of whispered observations of the physicians and his friends, which, from their tenor, were obviously not intended to reach the ears of the patient.

The paroxysms, after continuing for some time, began gradually to diminish in violence, the intervals becoming longer, and the duration of each spasm shorter, and it was hoped that they were about to pass off, when all at once they returned in their original violence. This proved, however, to be the last expiring effort of the poison; for

the symptoms now entirely ceased, about thirteen hours after the first dose was taken. At the conclusion of the spasms, the patient was left in an excessively exhausted state, and was unable to turn himself in bed; from this, however, he recruited with great rapidity, as he was able to get up on the evening of the next day, and on the second he walked out and went about his usual business. The most remarkable fact connected with the case is, that, from that time, the attacks of tic douloureux entirely ceased, and he has not since had any return of it. The medical treatment employed in the case was unimportant, and had not any effect on the progress of the symptoms.

On his recovery, it was immediately apparent to the patient that the supposed muriate of morphia was the cause of the symptoms from which he had suffered, and the remainder of it was sent to me for examination. On boiling it with water no solution took place, and the filtered fluid, when tested with nitrate of silver, was found to be free from hydrochloric acid. It was not therefore a muriate, and, considering the symptoms which it had produced, I at once applied to it the tests for strychnia. I found, that when treated with sulphuric acid containing a small quantity of nitric acid, and then mixed with peroxide of lead, it gave the characteristic violet tint described by Marchand.[1] A solution in muriatic acid gave, with sulphocyanide of potassium, the long needles described by Notus,[2] and under the microscope were obtained the characteristic crystals of strychnia, which will be described in the sequel of this paper. When treated with nitric acid it acquired a very feeble red colour. It dissolved entirely in acids, and burnt off with the exception of a very minute quantity of a white ash. From these observations, I infer that the substance was strychnia in a tolerably pure state; in fact, exactly such as is usually made use of in medicine.

The case which I have just detailed, is interesting in several points of view. In the first place, we have the perfect authentication of the quantity swallowed, the patient having himself weighed out the doses, together with the determination of the nature of the poison. Secondly, It is so far, as I have been able to ascertain, by much the largest dose from which recovery has been recorded. In general, a dose of one or two grains, and in the case of nux vomica itself, of which we have the largest number of cases, a quantity corresponding to not more than one-third of a grain of strychnia, has proved rapidly fatal. Indeed, a case is mentioned by Hoffmann[3] in which the death of a girl, ten years of age, was occasioned by two 15 grain doses of the nut, which contain about 0·15 grains of strychnia. It appears, however, that both strychnia and nux vomica present very great irregularity in the quantity required to produce their poisonous effects; the dose which has proved fatal in one case, being taken with impu-

[1] Journal de Pharmacie, N. S., Vol. IV. p. 200.
[2] Ibid., Vol. XXIV. p. 192.
[3] Hoffmannus, Philosophia Corporis Humani, Part II. Cap VIII.

nity in another. Dr Pereira[1] mentions a case in which he gave several one and a half grain doses of strychnia before its physiological effect was produced; and the older physicians, according to Sennertus,[2] were in the habit of administering the nut in doses of one or two scruples, and even in larger quantities, as a remedy for plague, a dose which would not be considered very safe at the present day. As a contrast with these quantities, I may state that the dose of strychnia taken in the case above detailed, corresponds to nearly three ounces of nux vomica.

Thirdly, The case is interesting from the slow and gradual approach of the symptoms, and the long period which elapsed before tetanic spasms supervened. In fact, the first dose of three and a half grains produced no symptoms except the want of power of the muscles, and no tetanic spasm occurred till after the second dose; and it may, I think, be fairly inferred, that if the second quantity had not been taken, the effects of the first might have gone off without producing any symptoms of greater severity than those observed during the first five hours. The instant, however, that the second dose was swallowed, the full violence of the symptoms was produced in the system, already partially under the influence of the poison. The question may be raised as to how far the action of the strychnia may have been affected by the habitual use of large quantities of opium; but I am not aware of any facts which can be directly brought to bear upon this point. The only case at all resembling it is one mentioned in the *Journal de Pharmacie*,[3] in which a pharmaceutical student of dissipated habits swallowed two grammes (about thirty-one grains) of strychnia on leaving a public place where he had been drinking, and in which tetanic spasms did not make their appearance till after a considerable period; so much so, that the physician, in the absence of all bad symptoms, refused to believe the reiterated assurances of the patient that he had actually taken it. In this case, it is just possible that intoxication may have prevented the immediate access of the symptoms, exactly as it is known to do in the case of poisoning by opium.

Fourthly, The perfect cure of the neuralgic symptoms, which, I find from the patient, has been permanent. He is also impressed with the idea, that the violent action of the poison has had a permanent effect upon the nervous system, as, since his recovery, he has been excessively nervous, easily startled and affected by trifles, which he never was before. I am inclined to attribute this, however, entirely to imagination, and the alarm naturally produced by the violent symptoms from which he has suffered.

In examining the substance which caused the symptoms already detailed, I was, of course, enabled to infer the probability of its being

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[1] Materia Medica.
[2] Sennertus, Medecina Practica, p. 1310, Lib. VI. Pars VII. Cap. XX.
[3] Journal de Pharmacie, N. S. Vol. X. p. 36.

strychnia, and to apply at once the direct tests for that substance, which, it fortunately happens, are much more delicate and characteristic than those which we possess for almost any of the other alkaloids. I have found Marchand's[1] test a very good one, and possessed of a considerable amount of delicacy; and, as I do not recollect to have seen it mentioned in any of our medical periodicals, although it has been known for some years, I may simply state, that it consists in pouring upon the strychnia a few drops of strong sulphuric acid, mixed with about one per cent of nitric acid, and then adding a small quantity of peroxide of lead, when immediately a fine violet colour is produced. The experiment succeeds best when the mixture is made in a watch glass, care being taken that the quantity of peroxide be extremely small, and then, on mixing with a glass rod, the colour makes its appearance in streaks. Bichromate of potass has been recommended by Otto,[2] and the results may be obtained by means of it; but not, so far as I have observed, so readily as with the peroxide of lead. The sulphocyanide test has been very little attended to by chemists, under the impression that the results are not to be depended upon, as some of the other alkaloids are also precipitated by that reagent; but none of them are capable of giving the immediate precipitate of long needles, which is obtained even from very dilute solutions of the salts of strychnia. In all the other alkaloids, the precipitate occurs only after the lapse of some time, and by shaking the solution, and then always in microscopic crystals, unless the solution have been extremely dilute and left in repose for twenty-four hours, when sometimes crystals, the form of which can be distinguished by the naked eye, are obtained. It is, however, desirable that some more definite means of distinguishing these precipitates, and the alkaloids generally, should be obtained; and an attempt has been made by Lepage[3] to supply the deficiency, by observing the action of a current of chlorine gas, both upon the alkaloids and their sulphocyanides; but it does not appear that the reactions it affords are sufficiently distinct to enable us with certainty to discriminate them.

In endeavouring to solve this difficulty, I was led to make use of the microscope, with the view of ascertaining whether the crystalline forms of the alkaloids themselves, or of their sulphocyanides, might not afford characters by which they might be easily distinguished on the small scale; and the result of my experiments has been sufficient to convince me that their forms are, in reality, exceedingly distinct, and that they can be easily distinguished in very small quantities.

The method which I have employed, consisted in dissolving the alkaloid in dilute hydrochloric acid, and mixing the dilute solution on a glass plate, with ammonia of moderate strength if the alkaloid

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[1] Journal de Pharmacie, Vol. IV. p. 200.
[2] Journal für Praktische Chimie, Vol. XXXVIII. p. 511.
[3] Ibid., Vol. XXVI. p. 140.

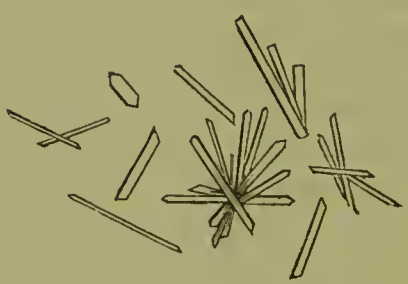
itself is to be examined; or with a strong solution of sulphocyanide of potassium if the sulphocyanide is required, and at once placing it under the microscope. The only precaution requisite is to avoid having the solution too concentrated, as the crystals are then less well defined than if a dilute solution is employed; but a few trials easily enable the experimenter to ascertain the proper degree of dilution.

Strychnia.—The hydrochlorate of strychnia, treated with ammonia, gives an immediate precipitate, which, when examined by a magnifying power of 250 diameters, is found to consist entirely of minute prismatic crystals, all nearly of the same size, and very well defined. A large proportion of these are isolated; but there is also a sort of twin crystal very abundant, the two members of which cross each other at an angle of about 60 degrees. They present, also, a sort of sulcated depression at opposite ends, which is very characteristic. They are represented in Fig. 1. The sulphocyanide of strychnia consists of flattened needles, sometimes single, but generally in irregular groups, as represented in Fig. 2. They are terminated either by

Fig. 1.



Fig. 2.



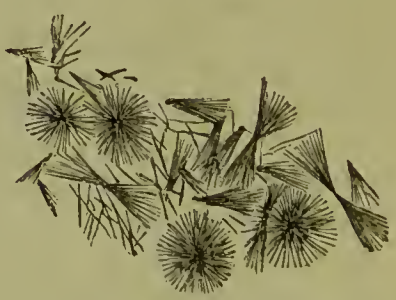
a blunt acumination or by a truncated extremity. Those which were precipitated on the large scale, were found to present the latter form.

Brucia.—A salt of brucia, in a sufficiently dilute state, mixed with ammonia, is found not to give an immediate precipitate; but,

Fig. 3.



Fig. 4.



in the course of a very short time, irregular star-like groups of pointed crystals are observed, which are represented in Fig. 3. With sulphocyanide of potassium, in a pretty strong solution, a precipitate is obtained in tufts of extremely thin and feathery crystals, which either radiate from a centre or present a sheaf-like appearance (Fig.

4). The latter form is, however, much better marked in the crystals deposited, after some hours, from a dilute solution, which are still quite microscopic, although somewhat larger than those represented in the figure.

Morphia.—In solutions of morphia, ammonia produces no precipitate at the moment of mixture; but, in the course of a longer or shorter period, according to the degree of dilution, crystals are seen to form, which gradually increase in size, and possess the form represented in Fig. 5. Salts of morphia are not precipitated by sulphocyanide of potassium, unless the solution be highly concentrated.

Narcotine—is precipitated by ammonia in branched groups of crystals of a pointed form (Fig 6). In concentrated solutions, a preci-

Fig. 5.

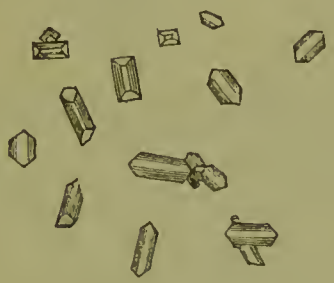


Fig. 6.



pitate is thrown down by sulphocyanide of potassium, which dissolves readily in hot water, and is deposited again on cooling. Under the microscope it is found to be perfectly amorphous.

Cinchonine—is obtained by precipitation with ammonia, in the form of minute granular masses, made up of more or less distinctly acicular crystals, radiating from a centre. It is, however, a little difficult to obtain them well marked, and they not unfrequently appear as a confused mass of granules, in which the radiated structure is very

Fig. 7.

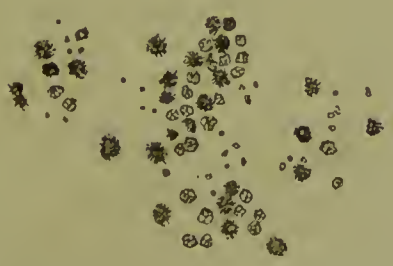
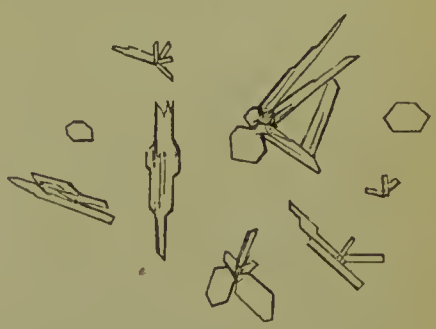


Fig. 8.



imperfectly seen. They form best when the solutions are rapidly mixed. Fig. 7 represents these crystals. With sulphocyanide of potassium, cinchonine gives a precipitate consisting of six-sided plates, together with a variety of irregular crystalline masses, and a few rectangular plates (Fig. 8). When formed by mixing in a test tube, with agitation, and allowing it to stand for some time, the crystals are still microscopic, but much more definite, and some-

times consist almost entirely of isolated six-sided tables, of great regularity. The precipitate dissolves readily in hot water, and is deposited, as the solution cools, in irregular plates.

Quinine—gives, with ammonia, a perfectly amorphous precipitate, but with sulphocyanide of potassium it gives small irregular groups of acicular crystals, which bear a resemblance to those produced by strychnia, but are longer and more irregular (Fig. 9). When the precipitate is produced in a test tube, and with a concentrated solution, it falls immediately as a white powder composed of extremely minute needles; but when the solution is dilute, it is deposited, after the lapse of twenty-four hours, in crystals from a quarter to a third of an inch in length. Lepage, under the same circumstances, states that he obtained a mass of yellowish green crystals, but I have always obtained them perfectly white. This is, of all those which I have examined, the salt which approaches most nearly in its characters to the strychnia compound, but it differs from it in the length of time required for its production in a dilute solution; and if we combine with its characters the amorphous precipitate which quinine affords with ammonia, we are able at once to distinguish the one base from the other.

Fig. 9.



Bebeerine—is precipitated amorphous both by ammonia and sulphocyanide of potassium. The latter precipitate is formed even in highly dilute solutions at the instant of mixture, and is a delicate test of the presence of that alkaloid, although quite inapplicable as a means of distinguishing it from others.

Atropine—is precipitated in the amorphous state by ammonia, and not at all by sulphocyanide of potassium.

It must be obvious from the observations now detailed, that under the microscope the forms of the different alkaloids examined are very characteristic and distinct, and that the combined observation of the base itself and of its sulphocyanide, may be considered as perfectly distinctive of the common alkaloids. I have not yet, however, had time to ascertain how far the method may be applicable to the detection of the substances containing those alkaloids, by extracting them with an acid, and examining the precipitates obtained from the fluid. It is unquestionable, however, that the regularity of the crystals would under such circumstances be impaired, although it is possible that their characteristics might be retained with sufficient completeness. However this may be, any addition to the tests for the pure alkaloids is a matter of importance; and I think the present communication may not be altogether without value, as adding something to the means of distinguishing a class of substances so poorly characterised by their ordinary chemical reactions as the organic alkalies.